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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
MOORE, WILLIAM W	
ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/884,455	HOUGHTON ET AL.	
	Examiner	Art Unit	
	WILLIAM W. MOORE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,31 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,31 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20090914*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 September 2009 has been entered, cancelling claims 28-30 and 32-35 and amending the remaining claims 27, 31, and 36 to describe compositions comprising either of two, particular, disclosed polypeptides and an assay method.

The claim amendments and cancellations remove the bases for the rejections of record of claims 27 and 31 herein under the first paragraph of 35 U.S.C. § 112 for lack of enablement and lack of adequate written description, and also remove the bases for the rejection of record of claims herein under 35 U.S.C. § 112, second paragraph and these rejections are, accordingly, WITHDRAWN. The claim amendments also remove the bases for the rejections of record of claims herein over the claims of U.S. Patent No. 5,712,145 based on nonstatutory double patenting and these rejections are also WITHDRAWN. Because the applications 10/409,094 and 10/409,673 are no longer pending, the rejections of record of claims herein over the claims of those applications based on nonstatutory double patenting rejection are MOOT.

Information Disclosure Statement

Applicant's Information Disclosure Statement [IDS] filed with the request for continued examination filed on 14 September 2009 is hereby acknowledged. Executed copies of the seventy-four pages of PTO Forms-1449 citing documents that, in most instances, cite documents cited and supplied in the prosecution of application 10/438,313, accompany this communication. Those citations that are duplicative of citations made elsewhere in the IDS, or made in the PTO-Form 892 mailed with the communications of 1 July 2004, 12 April 2005, and 12 January 2006 are lined-through to prevent duplication in the publication of any patent that may issue on the instant application.

Claim Objections

Claim 36 is objected to because of the following informalities: Claim 36 improperly recites "[a] method . . . for activity against the purified [hSOD-NS3 domain fusion] polypeptide of claim 31, and clauses (a) – (c) of claim 36 all also recite "purified polypeptide", because claim 31 is drawn instead to a "composition comprising" the hSOD-NS3 domain fusion polypeptide of SEQ

ID NO:86. Claim 36 as currently amended can properly refer back only to a claim that describes a "purified polypeptide" but may be further amended to avoid this objection by instead reciting, "activity against the polypeptide comprised by the composition of claim 31 comprising . . . providing the composition of claim 31". Appropriate correction is required.

Double Patenting: Non-Statutory

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 27 remains rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,585,258. Applicant's arguments at page 4 of the Remarks filed 14 September 2009 have been fully considered but are not persuasive. Applicant suggests that the amendment of claim 27 avoids the rejection of record because claim 27 now requires the entire 686-amino acid sequence of the HCV NS3 domain taught in Figure 1 of the patent, thus is no longer a generic embodiment of the patented claim 1 and "not obvious over the claims in the issued patent[ ]". This is not persuasive where the patented claim 1 describes a composition that comprises a polypeptide that may comprise the 686-amino acid HCV NS3 domain as taught by Figure 1 of the patent. Where the patent specification particularly teaches that the entire NS3 domain polypeptide of amended claim 27 herein is a preferred embodiment of the patented claim 1, the subject matter of the currently amended claim 27 would be obvious to the artisan. The rejection of record herein is therefore maintained until and unless an effective terminal disclaimer is filed.

Claim 31 remains rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 5 of U.S. Patent No. 5,585,258 in view of Benson et al. U.S. Patent No. 5,258,496. The teachings of Benson et al., discussed in the rejection of record are taken as before. Applicant's arguments at page 4 of the Remarks filed 14 September 2009 have been fully considered but are not persuasive. Applicant suggests that the amendment of claim 31 avoids the rejection of record because claim 31 now

requires the 841-amino acid sequence of the fusion polypeptide taught in Example 4 (A) of the patent specification, thus is no longer a generic embodiment of the patented claim 5 and "not obvious over the claims in the issued patent[ ]". This is not persuasive where the patented claim 5 describes a polypeptide that may comprise the 686-amino acid HCV NS3 domain, see, e.g., Figure 1 of the patent that depicts the NS3 domain polypeptide amino acid sequence of SEQ ID NO:70, fused at its amino terminus to the carboxyl terminus of the first 155 amino acids of the amino acid sequence of hSOD as taught by Example 4(A) of the patent specification and taught as well in the patent's Figure 10 depicting the amino acid sequence of SEQ ID NO:86. Where the patent specification particularly teaches that the amino acid sequence of SEQ ID NO:86 now described by claim 31 herein is a preferred embodiment of the patented claim 5, and Bensen et al. teach that recombinantly-produced fusion proteins are ordinarily comprised in compositions during purification from a host cell wherein they are expressed, the subject matter of the currently amended claim 31 would be obvious to the artisan. The rejection of record herein is therefore maintained until and unless an effective terminal disclaimer is filed.

Claim 36 remains rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,597,691. Applicant's arguments at page 4 of the Remarks filed 14 September 2009 have been fully considered but are not persuasive. Applicant suggests that the amendment of claim 36 avoids the rejection of record because claim 36 now requires that an assay be conducted with the fusion polypeptide that has the 841-amino acid sequence taught in Example 4 (A) of the patent specification, thus is no longer a generic embodiment of the patented claim 1 and "not obvious over the claims in the issued patent[ ]". This is not persuasive where the patented claim 1 describes an assay conducted according to Example 4(A) of the patent specification that itself utilizes the same fusion polypeptide having the amino acid sequence of SEQ ID NO:86 that is also taught in Figure 10 of the patent specification. Where the patent specification particularly teaches that an assay for an inhibitor of the amino acid sequence of SEQ ID NO:86 should be conducted with the polypeptide of SEQ ID NO:86 and is a preferred embodiment of the patented claims, the subject matter of the currently amended claim 36 would be obvious to the artisan. The rejection of record herein is therefore maintained until and unless an effective terminal disclaimer is filed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable

> any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36 remains rejected for reasons of record under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant's arguments at pages 4 and 5 of the Response have been fully considered but they are not persuasive to overcome the rejection of record of claim 36. The disclosure must establish Applicant's possession, at the time the disclosure was originally filed, of an assay as defined in claim 36 for detecting inhibitors of such a proteolytically active polypeptide. Claim 36, if properly stated, would require that an assay for detecting inhibitors of the fusion protein of SEQ ID NO:86 be conducted in a composition that also comprises an inhibitor yet, in order to produce any measurable results, the assay composition must also comprise a substrate, the cleavage of which can be measured to determine whether or not it decreases, where a decrease in proteolytic activity permits detection of an inhibitor. The specification's Examples 4 and 5 provide the "P600" fusion polypeptide, see Example 4 (A) with the amino acid sequence set forth in SEQ ID NO:86 and Applicant had asserted at pages 6 and 9-15 of the Response filed 15 May 2008 that this particular fusion protein comprising the entire NS3 domain may have an "NS2/NS3" proteolytic activity. But the specification does not contemplate such activity and there is no disclosure in the specification that NS2/NS3 cleavage, essentially an autocatalytic activity occurs. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano,* 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The NS2/NS3 autocatalytic metalloprotease activity takes place at a region of the HCV polyprotein that is absent from the NS3 domain of SEQ ID NO:70 within the P600 fusion protein of SEQ ID NO:86, and the carboxyl-proximal region of the NS2 domain where NS2/NS3 cleavage occurs was discovered after the filing date of the original disclosure of the present specification, thus could not reasonably considered by the artisan to have been in Applicant's possession at the time the specification was originally filed. Applicant also asserted at page 6 of the Response 15 May 2008 that an NS3 serine protease activity is disclosed in Examples 10 and 11 but the specification identifies no region within the NS3 domain amino acid sequence constituting the carboxyl-proximal 80% of the amino acid sequence of SEQ ID NO:86 where proteolysis occurs, and does not discuss or suggest a serine protease activity of the integral NS3 domain.

The "test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the Inventor had possession at that time of the . . . claimed subject matter", *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983). None of the HCV polyprotein regions that Sardana et al. report to be substrates that cleaved by an HCV NS3 serine protease are disclosed or suggested in the specification and all of these regions are absent from the P600 protein of Examples 4 and 5. Applicant cited publications of Vishnuvardhan et al. and Barbato et al., made of record with Applicant's IDS, in the Response filed 15 May 2008 but Applicant did not then, and does not now, suggest that the P600 fusion protein comprises any region of the HCV polyprotein that could serve as a self-substrate for P600 fusion polypeptide purportedly cleaved in Example 5. The cleavage sites Applicant cites at pages 7 and 8 of the Response filed 15 May 2008 where an integral NS3 domain protease might act without assistance of the NS4A peptide that were subsequently identified by Lin et al., 1994, Bartenschlager et al., 1994, and Bartenschlager et al., 1995, all now of record herein, are not present in SEQ ID NO:86. Where none are present, even in the P600 construct, the specification cannot be considered to have disclosed Applicant's possession of a NS3 domain serine protease. Applicant presented an ancillary argument at pages 10 and 11 of the Response 15 May 2008 urging that the presence of human superoxide dismutase [hSOD] as an amino-proximal fusion partner reconstitutes a NS2/NS3 autocatalytic cleavage but this is unpersuasive because the mass of the cleavage fragment produced does not indicate that the cleavage was produced by HCV NS2/3 autocatalytic activity and such proteolytic activity, when it occurs in a naturally-occurring HCV polyprotein, is not a serine protease activity. The rejection of record is therefore maintained.

Claims 36 remains rejected for reasons of record 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for conducting an assay that might detect an inhibitor of the P600 fusion protein of SEQ ID NO:86 where there the specification teaches no substrate for a proteolytic activity that might be measured in order to detect inhibition of a proteolytic activity of a P600 fusion protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Applicant's arguments at page 5 of the Response filed 14 September 2009 have been fully considered but they are not persuasive. Applicant had previously suggested, at pages 16-19 of the Response filed 15 May 2008, that the specification enables the preparation of a NS2/NS3 domain protease that might arise due to a fusion with hSOD. The specification itself, however, teaches away from the preparation of anything other than a serine protease and provides no guidance that could help the artisan select the portion of the NS2 domain that must be included

together with the NS3 domain amino acid sequence within the P600 fusion protein in order to conduct an autocatalysis. Indeed, the native NS2/NS3 autocatalytic of an HCV polyprotein was disclosed by others only after the application was filed. Applicant had also proposed at pages 19-21 of the Response filed 15 May 2008 that the specification discloses an adequate substrate, "in the form of [the] HCV polyprotein" with which experimentation might be conducted, and that its use "for testing NS3 serine protease activity in *trans*", might require no undue experimentation on the part of the artisan to make HCV NS3 domain proteases commensurate in scope with the recitations of the claims rejected herein. With regard to what may constitute "undue experimentation", the CCPA, the precursor of the Court of Appeals for the Federal Circuit, determined that a **reasonable correlation** must exist between the **scope asserted** in the claimed subject matter and **the scope of the guidance** the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (emphasis supplied). The Federal Circuit approved the standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Instead, the P600 fusion protein of SEQ ID NO:86 includes no amino acid sequence region that permits cleavage at the NS2/3 junction by a NS2/3 metalloprotease and includes none of the amino acid sequence regions, e.g., the NS3/4A, NS4A/4B or NS4B/5A junctions, where an Hepatitis C Virus NS3 domain serine protease cleaves. The specification provides no guidance that might direct the artisan to select the HCV NS5 domain as a substrate for serine protease activity. Indeed, the only substrates that the specification proposes, e.g., at pages 19-21 therein as discussed in the communication mailed 16 November 2007, are not the substrates of the NS3 domain serine protease within SEQ ID NO:86. Where the specification provides no guidance as to what more might be required for a claimed method beyond the particular P600 fusion protein having the amino acid sequence of SEQ ID NO:86, e.g., how to locate the sequence of NS4A cofactor, a region absent from SEQ ID NO:86, the specification fails to indicate the direction the artisan might take to begin the next, necessary, process of experimentation. The rejection of record is therefore maintained.

Conclusion

No claim is allowed but cancellation of claim 36 and the submission of Terminal Disclaimers over the terms of US Patent No. 5,585,258 may permit allowance of claims 27 and 31 herein.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See

MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Andrew Wang, can be reached at 571.272.0811. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/William W. Moore/
Examiner, Art Unit 1656

/ANAND U DESAI/
Primary Examiner, Art Unit 1656
September 30, 2009